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National Institute of Mental Health
Addiction Research Center
U.S. Public Health Service Hospital
Lexington, Kentucky

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

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I am enclosing herewith copies of three tables: "Comparison of the total course of the LSD, mescaline and psilocin reactions," "Mean increase in pupillary diameter over control," and "Mean increase in number positive answers over control." All drugs were given intramuscularly, a departure from our previous practice. The 10 subjects used received all drugs. The methods used were those that have become standard with us for psychotomimetic studies. The experiments were done partly to get equivalent dosages of LSD and mescaline, and also to get some information on psilocin (dephosphorylated psilocybin).

As expected, the effects of all three drugs were quite similar quantitatively. All three induce the same sort of autonomic changes including pupillary dilatation, temperature elevation, blood pressure rise, etc., and all induce similar mental changes including alterations in mood, body image, sensory distortion and hallucinations, chiefly of the visual type. The chief differences relate to potency and time course.

As is apparent from the tables, the onset of the psilocin reaction is quite rapid, nearly maximal effect being attained in the first half-hour. After 2-1/2 hours the psilocin reaction is already declining sharply, and after 3-1/2 to 4-1/2 hours has declined to negligible proportions. It is of some interest that psilocin is the most consistent agent we have studied, insofar as the induction of hallucinations is concerned. All 10 men who received a 150-mcg/kg dose had hallucinations and 9 of them lost insight. Despite this, psilocin seems less unpleasant than either LSD or mescaline, perhaps because of the short time course.

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The calculation of relative potency presents something of a problem because of the marked difference in the time courses. The relative slowness and long persistence of the mescaline reaction should be noted in this regard. However it is apparent that 1.5 mcg/kg of LSD is equivalent to 75 mcg/kg of psilocin substance and to 5000 mcg/kg of mescaline hydrochloride.

Currently we are running a small study on the relative potency of psilocin and psilocybin. Psilocin is of course more potent in terms of weight, but probably there will be very little difference in terms of moles.

Cross tolerance between mescaline and LSD is well along and I feel almost certain that a high grade of cross tolerance will exist. Amphetamine is next on the agenda insofar as cross tolerance is concerned.

It was very pleasant to see you during my last trip to Washington, and I am sending kindest personal regards for the New Year.

Sincerely yours,

Harris
Harris

HL:bws

Enclosures
Tables (3)

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Comparison of the total course of the LSD, mescaline, and psilocin reactions

Drug	Dose	Pernometer					Threshold for Knee Jerk	Positive Anxiety	Clinical Grade
		Temp. 1 (°C.)	Pulse 1	Blood Pressure 1 (mm)	Pupils 1 (mm)				
LSD-25	0.75 mcg/kg	+3.43 ± 0.41	+53.15 ± 10.18	+45.50 ± 12.46	+ 7.08 ± 0.89	-54.25 ± 11.01	37.10 ±	4.67	1.03
" 25	1.50 mcg/kg	+4.31 ± 0.42	+66.03 ± 7.70	+56.20 ± 10.10	+12.90 ± 1.61	-54.00 ± 0.69	72.35 ± 11.09	2.45	2.45
" mescaline	2.5 mcg/kg	+3.40 ± 0.41	+33.40 ± 9.27	+45.46 ± 13.63	+12.40 ± 1.62	-65.50 ± 15.06	35.00 ±	5.94	1.03
" mescaline	5.0 mcg/kg	+4.56 ± 0.36	+71.10 ± 17.70	+76.95 ± 12.46	+17.33 ± 1.93	-73.00 ± 16.80	67.15 ± 13.03	2.10	2.10
" psilocin	37.5 mcg/kg	+3.85 ± 0.44	+37.25 ± 10.00	+32.85 ± 14.93	+ 6.54 ± 1.16	-47.56 ± 15.74	12.10 ±	4.66	1.03
" psilocin	75 mcg/kg	+4.30 ± 0.42	+16.56 ± 12.41	+41.35 ± 10.51	+ 6.74 ± 0.83	-33.56 ± 0.19	49.00 ±	7.32	2.55
" psilocin	150 mcg/kg	+5.17 ± 0.25	+41.10 ± 12.29	+57.20 ± 10.43	+14.56 ± 1.53	-67.83 ± 17.12	84.10 ±	6.44	3.00

1. Figures are the means (10 subjects) ± standard errors of areas under time-action curves ("degree-hours," "rate-hours," etc.). The signs indicate increases (+) or decreases (-) in the measurements.
2. Means ± standard errors of number of questions scored positively in the 7-1/2 hours after the drug which were not scored positively before the drugs.
3. Means ± standard errors of intensity of mental reaction on a scale of 0-4.

Mean Increase in Pupillary Diameter (mm) over Control

Drug	Dose	Hours after Administration of Drug							
		1	2	3	4	5	6	7	8
LSD-25	0.75 mcg/kg	+1.32	+1.78	+1.63	+0.88	+0.82	+0.53	+0.62	+0.73
LSD-25	1.50 mcg/kg	+1.85	+2.55	+2.40	+1.90	+1.45	+1.20	+1.15	+0.80
Mescaline	2.5 mg/kg	+1.55	+1.65	+1.65	+1.55	+1.25	+1.05	+1.00	+1.00
Mescaline	5.0 mg/kg	+2.20	+2.75	+2.75	+2.55	+2.15	+2.00	+2.00	+1.85
Psilocin	37.5 mcg/kg	+1.93	+2.02	+1.08	+0.68	+0.62	+0.28	+0.02	-0.05*
Psilocin	75.0 mcg/kg	+2.43	+2.33	+1.93	+0.92	+0.48	+0.32	+0.33	+0.42
Psilocin	150 mcg/kg	+3.73	+3.82	+2.72	+1.73	+1.12	+0.63	+0.43	+0.33

* Represents only item in table with negative sign

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Mean Increase in Number Positive Answers over Control
N = 10

Drug	Dose	Hours after Administration of Drug							
		1 ^{1/2}	2 ^{1/2}	3 ^{1/2}	4 ^{1/2}	5 ^{1/2}	6 ^{1/2}	7 ^{1/2}	8 ^{1/2}
LSD-25	0.75 mcg/kg	4.20	13.10	11.70	5.70	2.20	0.20	0	0
LSD-26	1.50 mcg/kg	11.10	22.70	21.00	9.10	5.30	2.20	0.60	0.50
Mescaline	2.5 mg/kg	8.10	12.30	7.60	4.10	2.20	1.00	0.40	0.20
Mescaline	5.0 mg/kg	9.30	15.50	18.10	13.90	7.50	3.30	0.90	0.50
Psilocin	37.5 mcg/kg	8.00	7.00	3.50	0.60	0	0	0	0
Psilocin	75.0 mcg/kg	19.50	18.50	8.60	1.70	0.40	0.30	0	0
Psilocin	150.0 mcg/kg	30.90	34.90	20.30	8.40	1.60	0	0	0

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